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FILE COVERS 1907 - 8 May 2003 VOL 138 ISS 20 FILE LAST UPDATED: 8 May 2003 (20030508/ED)

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=> s (early pregnancy factor?) or (early conception factor?)

316876 EARLY

75852 PREGNANCY

1220359 FACTOR?

130 EARLY PREGNANCY FACTOR?

(EARLY (W) PREGNANCY (W) FACTOR?)

316876 EARLY

7251 CONCEPTION

1220359 FACTOR?

2 EARLY CONCEPTION FACTOR?

(EARLY (W) CONCEPTION (W) FACTOR?)

L1 132 (EARLY PREGNANCY FACTOR?) OR (EARLY CONCEPTION FACTOR?)

=> s l1 and antibod?

365755 ANTIBOD?

L232 L1 AND ANTIBOD?

=> d ti ab 1-32

L2ANSWER 1 OF 32 CA COPYRIGHT 2003 ACS

ΤI Bovine pregnancy test AB This invention provides bovine pregnancy test methods and devices. The test is also suitable for other ruminant and/or ungulate animals. Antigens from Group A (early pregnancy antigens), and/or Group B (mid-pregnancy antigens), and Group C (early, mid- and late pregnancy antigens) are detected in a fluid from the animal, and pregnancy is reliably detd. The pregnancy assays of this invention are preferably carried out using immunoassay devices which provide immediate results in the field.

L2 ANSWER 2 OF 32 CA COPYRIGHT 2003 ACS

TΙ

AB

AΒ

\*\*\*Early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* peptides assays and therapeutic uses

The present invention provides assays for the study of the interaction of \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* (EPF) and EPF-related peptides with human dorsal root receptors (hDRR) -4 and -7. The assays are useful to identify whether a test compd. can bind to the hDRR under conditions in which EPF or related peptide can bind to the receptor and to det. whether the test compd. is an agonist or antagonist of hDRRs. Pharmaceutical compns. contg. the hDRRs agonists and antagonists, as well as \*\*\*antibodies\*\*\* of an hDRR binding fragment are also claimed. Addnl. claimed are hDRRs disorders diagnosis methods and methods to detect and isolate hDRR from cells and membrane prepns. and to identify and obtain a test compd. capable of modulating the activity of hDRRs. The uses of EPF-related peptides and compds. identified by the assays in pharmaceutical compds. to serve as contraceptives or in treatment of certain diseases like cancer and autoimmune disease are claimed.

L2 ANSWER 3 OF 32 CA COPYRIGHT 2003 ACS

TI Immunoelectron microscopy provides evidence for the presence of mitochondrial heat shock 10-kDa protein (chaperonin 10) in red blood cells and a variety of secretory granules

Hsp10 (10-kDa heat shock protein, also known as chaperonin 10 or Cpn10) is

a co-chaperone for Hsp60 in the protein folding process. This protein has also been shown to be identical to the \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* , which is an immunosuppressive growth factor found in maternal serum. In this study we have used immunogold electron microscopy to study the subcellular localization of Hsp10 in rat tissues sections embedded in LR Gold resin employing polyclonal \*\*\*antibodies\*\*\* against different regions of human Hsp10. In all rat tissues examd. including liver, heart, pancreas, kidney, anterior pituitary, salivary gland, thyroid, and adrenal gland, \*\*\*antibodies\*\*\* to Hsp10 showed strong labeling of mitochondria. However, in a no. of tissues, in addn. to the mitochondrial labeling, strong and highly specific labeling with \*\*\*antibodies\*\*\* was also obsd. in several the Hsp10 extramitochondrial compartments. These sites included zymogen granules in pancreatic acinar cells, growth hormone granules in anterior pituitary, and secretory granules in PP pancreatic islet cells. Addnl., the mature red blood cells which lack mitochondria, also showed strong reactivity \*\*\*antibodies\*\*\* . The obsd. labeling with the Hsp10 with the Hsp10 \*\*\*antibodies\*\*\* , both within mitochondria as well as in other compartments/cells, was abolished upon omission of the primary

\*\*\*antibodies\*\*\* or upon preadsorption of the primary \*\*\*antibodies\*\* with the purified recombinant human Hsp10. These results provide evidence that similar to a no. of other recently described mitochondrial proteins (viz., Hsp60, tumor necrosis factor receptor-assocd. protein-1, P32 (gClq-R) protein, and cytochrome c), Hsp10 is also found at a variety of specific extramitochondrial sites in normal rat tissue. These results raise important questions as to how these mitochondrial proteins are translocated to other compartments and their possible function(s) at these sites. The presence of these proteins at extramitochondrial sites in normal tissues has important implications concerning the role of mitochondria in apoptosis and genetic diseases.

ANSWER 4 OF 32 CA COPYRIGHT 2003 ACS TI\*\*\*antibodies\*\*\* which neutralize the activity of Isolation of \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* \*\*\*Early\*\*\* \*\*\*preqnancy\*\*\* \*\*\*factor\*\*\* AB(EPF) is a secreted protein with growth regulatory and immunomodulatory properties. functions as an autocrine growth factor for tumor cells and as an autocrine or paracrine growth factor for regenerating normal cells. \*\*\*antibodies\*\*\* have demonstrable anti-tumor activity and, as a result, hybridomas which produce such \*\*\*antibodies\*\*\* unstable. In this study, the phage display \*\*\*antibody\*\*\* techniques have been investigated as a means of producing recombinant anti-EPF \*\*\*antibodies\*\*\* . Mice were immunized with synthetic peptides which correspond to the N or C terminal regions of EPF, and their splenic tissue \*\*\*antibody\*\*\* was used to make combinatorial libraries. The Fab repertoire was displayed on the surface of phage and panned over recombinant EPF. Reactive Fabs were identified by ELISA and their binding was characterized by BIAcore anal. and functional studies. libraries with a size of greater than 5.times.107 cfu were constructed and a total of 26 unique Fabs with specific reactivity against EPF were identified. Three Fabs were purified and of these one demonstrated strong EPF neutralizing activity, one had intermediate activity and the other was not neutralizing. Phage display has provided the means of circumventing the problems of anti-EPF hybridoma development and has resulted in the \*\*\*antibodies\*\*\* with potential applications in the diagnosis of pregnancy and the diagnosis and therapy of cancer.

- L2 ANSWER 5 OF 32 CA COPYRIGHT 2003 ACS
- TI Antagonists of chaperonin 10
- AB An antagonist to, or an \*\*\*antibody\*\*\* (Ab) raised against, cpn10 or a recombinant cpn10 with the sequence: GSAGQAFRKFLPLFDRVLVERSAAETVTKGGIMLPEK SQGKVLQATVEAVGSGSKGKGGEIQPVSVKEGDKVLLPEYGGTKVVLDDKDYFLFRDGDILGKYVD is claimed. Also, claimed are: (1) an antagonist or Ab raised against a peptide derived from cpn10, or a peptide with the sequence: Ac-AGQAFRKLPL(C), AGQAFRKFLPLA2, A1AGQAFRKFLPL, Ac-A1AGQAFRKFLPL, (A1) EKSQGKVLQATA2, and A1EKSQGKVLQAT where A1 and A2 are amino acid sequences that may be added to one or both ends of the peptides, and where the peptides may have a single amino acid deletion, addn. or substitution; (2) suppressing cellular growth or enhancing immunol. activity by administration of a cpn10 antagonist or anti-cpn10 Ab to a subject; and (3) an assay for measuring anti-cpn10 Ab in a sample by: (a) reacting purified cpn10 with the sample (b) detg. the amt. of Ab in the sample by detg. the binding between the Ab and cpn10. The cpn10 antagonist or Ab can be used to terminate pregnancy, suppressing tumor cell growth or enhancing the immune system.
- L2 ANSWER 6 OF 32 CA COPYRIGHT 2003 ACS
- TI Preparation and characterization of polyclonal \*\*\*antibodies\*\*\* against human chaperonin 10
- AB \*\*\*Early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* (EPF) has been identified as an extracellular homolog of chaperonin 10 (Cpn10), a heat shock protein that functions within the cell as a mol. chaperone. Here, we report the prodn. of polyclonal \*\*\*antibodies\*\*\* directed against several different regions of the human Cpn10 mol. and their application to specific protein quantitation and localization techniques. These

\*\*\*antibodies\*\*\* will be valuable tools in further studies to elucidate the mechanisms underlying the differential spatial and temporal localization of EPF and Cpn10 and in studies to elucidate structure and function.

Tunccion

- L2 ANSWER 7 OF 32 CA COPYRIGHT 2003 ACS
- TI Method and apparatus for detecting conception in animals using \*\*\*antibodies\*\*\* to \*\*\*early\*\*\* \*\*\*conception\*\*\*
- AB The present invention provides \*\*\*antibodies\*\*\* which specifically

\*\*\*early\*\*\* \*\*\*factor\*\*\* , which can be \*\*\*conception\*\*\* found in body fluids of animals including but not limited to the cow, cat, dog, horse, human, sheep, and pig. The invention provides methods for detecting conception or the absence of conception in an animal, the latter being recognized by the absence of \*\*\*early\*\*\* \*\*\*conception\*\*\* in a suitable body fluid collected from the animal. \*\*\*factor\*\*\* \*\*\*early\*\*\* \*\*\*conception\*\*\* Apparatus for detecting in a body fluid from an animal comprising the \*\*\*antibodies\*\*\* which specifically bind \*\*\*early\*\*\* \*\*\*conception\*\*\* \*\*\*factor\*\*\* are also provided.

L2 ANSWER 8 OF 32 CA COPYRIGHT 2003 ACS

TI Application of anti-bovine CD2 monoclonal \*\*\*antibody\*\*\* to the rosette inhibition test for detection of \*\*\*early\*\*\* \*\*\*pregnancy\*\*\*

\*\*\*factor\*\*\* in cattle

\*\*\*early\*\*\* \*\*\*factor\*\*\* To reliably detect \*\*\*pregnancy\*\*\* (EPF) in cattle, monoclonal \*\*\*antibody\*\*\* specific for bovine CD2 mol., which is the sheep red blood cell (SRBC) receptor on bovine T cell surface, was applied to the rosette inhibition test. The rosette inhibition titers (RITs) were higher in pooled sera from early pregnant cattle than in those of non-pregnant cattle using 2 anti-bovine CD2 \*\*\*antibodies\*\*\* , B26A4 and BAQ95A. The dissocn. value of RITs between pregnancy and non-pregnancy with B26A4 was greater than that with BAQ95A. The B26A4 monoclonal \*\*\*antibody\*\*\* was therefore applied to the rosette inhibition test in subsequent expts. The RITs in serum of individual pregnant and non-pregnant cows 8 days after estrus were different by .gtoreq.3 dilns. When the rosette inhibition test was carried out in sera from individual pregnant and non-pregnant cows at estrus and at 24, 72, and 168 h after ovulation, the RITs of pregnancy sera increased at 24 h after ovulation as compared with non-pregnancy Thus, anti-bovine CD2 monoclonal \*\*\*antibody\*\*\* can be utilized with the rosette inhibition test to detect EPF in cattle, and this assay detects bovine EPF in pregnancy serum at 24 h after ovulation.

- L2 ANSWER 9 OF 32 CA COPYRIGHT 2003 ACS
- TI Chaperonin 10

AB

- AΒ A process was developed for the detection of Chaperonin 10 (cpn10) in serum or other biol. fluids. The method involves several steps: (i) \*\*\*antibody\*\*\* to cpn10; (ii) reacting said \*\*\*antibody\*\*\* with a sample of biol. fluid suspected of contg. cpn10; and (iii) detecting the presence of cpn10 in said sample by a signal amplification resulting from prodn. of a cpn10- \*\*\*antibody\*\*\* complex. Cpn10 was discovered to be \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* Human cpn10 cDNA was cloned and expressed in E. coli. Recombinant cpn10 had the sequence GSAGQAFRKFLPLFDRVLVERSAAETVTKGGIMLPEKSQGKVLQATEVAVGSGSKGK GGEIQPVSVKEGDKVLLPEYGGTKVVLDDKDYFLFRDGDILGKYVD. Studies showed the beneficial effects of treatment with recombinant cpn10, including effects on allogenic skin grafts, wound healing, tissue repair, autoimmune disease, and infertility. Residues 1-11 and 34-44 in rat and human cpn10 were shown to be responsible for biol. activity. Various cpn10-derived peptides were synthesized and used to induce \*\*\*antibodies\*\*\* Neutralization of cpn10 in pregnancy serum by the \*\*\*antibodies\*\*\* adversely affected embryonic viability in the early stages of pregnancy.
- L2 ANSWER 10 OF 32 CA COPYRIGHT 2003 ACS
- TI Preparation of the monoclonal \*\*\*antibodies\*\*\* against human 
  \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\*
- In the present study, the authors report two hybridoma cell lines (1B6, 2F10) secreting monoclonal \*\*\*antibodies\*\*\* (McAbs). McAbs 1B6 and 2F10 were IgG1 and the no. of chromosomes of 2 hybridoma cell lines (1B6, 2F10) ranged from 100-106. The titer of the EPF McAbs in the ascites was 1:128,000 by ELISA. These McAbs against human EPF may be useful tools for

studying the biol. properties and function of human EPF.

L2

ΤI

AB

L2

TI

AΒ

ANSWER 11 OF 32 CA COPYRIGHT 2003 ACS \*\*\*Early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* in liver regeneration after partial hepatectomy in rats: Relationship with chaperonin 10 \*\*\*Early\*\*\* of dividing embryonic and neoplastic cells, as demonstrated previously, but also of normal proliferating cells. Eight hours after partial \*\*\*pregnancy\*\*\* hepatectomy in rats, \*\*\*early\*\*\* \*\*\*factor\*\*\* was detected in serum. It rose to a peak by 48 h. Neutralization of \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* in vivo by passive immunization with specific \*\*\*antibodies\*\*\* , 18 h after partial hepatectomy, resulted in a decrease in the uptake of [3H]thymidine by the liver remnant, measured 4-6 h later. Thus, during liver regeneration, \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* is essential to the sequence of events that culminates in DNA synthesis and cell division. Recently the authors purified \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* from human platelets and detd. by mass spectrometry a \*\*\*factor\*\*\* precise mol. mass of 10,843 Da. Amino acid sequencing (.apprx.72% of the \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* mol.) demonstrated that \*\*\*factor\*\*\* is highly homologous with chaperonin 10, a stress-inducible mitochondrial \*\*\*early\*\*\* protein, and that platelet-derived \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* and rat chaperonin 10 share similar biochem. and immunol. \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* properties. Here the authors show that \*\*\*factor\*\*\* , purified from regenerating rat liver and from serum taken 24 h after hepatectomy, shares these properties. In addn., to \*\*\*early\*\*\* \*\*\*antibodies\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* effective in passive immunization studies, recognize chaperonin 10, \*\*\*antibodies\*\*\* bind to whereas chaperonin 10 \*\*\*earlv\*\*\* \*\*\*factor\*\*\* \*\*\*pregnancy\*\*\* from regenerating liver and posthepatectomy serum. The authors propose that \*\*\*early\*\*\* \*\*\*factor\*\*\* /chaperonin 10 is selectively released \*\*\*prequancy\*\*\* from proliferating cells and, in an autocrine or paracrine mode (or both) is involved in DNA synthesis.

ANSWER 12 OF 32 CA COPYRIGHT 2003 ACS The purification of \*\*\*early\*\*\* - \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* to homogeneity from human platelets and identification as chaperonin 10 \*\*\*Early\*\*\* - \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* (EPF), first discovered in the early stages of gestation, is assocd. with and necessary for cell proliferation in a wide variety of biol. situations. Like many other growth factors, EPF is present in platelets, and, by titrn. studies with a neutralizing anti-EPF monoclonal \*\*\*antibody\*\*\* , platelets were identified as an extremely rich source of this growth factor. EPF has been purified from clin. outdated human platelets by heat extn., ion-exchange and affinity chromatogs. on SP-Sephadex and heparin-Sepharose resp., high-performance hydrophobic interaction chromatog. and three reverse-phase HPLC steps, with an av. yield of 15 .mu.g/100 platelet units (equiv. to .apprxeq. 50 L blood). Using SDS-PAGE, EPF migrated as a single band with approx. Mr 8500, coincident with biol. activity. Ma spectrometry provided an accurate and precise detn. of the mol. mass as Mr 10843.5, along with definitive evidence of the homogeneity of the prepn. Attempts at Edman degrdn. indicated that the mol. was blocked at the N-terminus and sequencing of proteolytic fragments was undertaken. amino acid sequence of approx. 70% of the mol. was detd. which, with a single exception, is identical with rat chaperonin 10. This structural relation was shown to extend to functional identity by studies using chaperonin 10 and its functional assoc. chaperonin 60. Investigations with the latter confirmed that chaperonin 10 is the moiety in pregnancy serum which initiates response in the EPF bioassay. The authors' studies identify EPF as a member of the highly conserved heat-shock family of mols. and demonstrate a mol. chaperone performing an extracellular role.

- L2 ANSWER 13 OF 32 CA COPYRIGHT 2003 ACS
  TI Study of \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* (EPF). 2
  AB A review, with 117 refs., on the prepn. of polyclonal and monoclonal
- AB A review, with 117 refs., on the prepn. of polyclonal and monoclonal

  \*\*\*antibodies\*\*\* specific for EPF for EIA, and hypotheses on the prodn.
  and action mechanism of EPF.
- L2 ANSWER 14 OF 32 CA COPYRIGHT 2003 ACS
- TI Detection of bovine \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\*
- (EPF) active polypeptide in different species of mammals

  AB The authors studied the cross-reactivity between bovine
  - The authors studied the cross-reactivity between bovine \*\*\*early\*\*\*

    \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* (EPF) and components in serum from

    females of 47 species by a monoclonal \*\*\*antibody\*\*\* (mab) capable of

    recognizing the EPF-active polypeptide in cattle to obtain data on the

    occurrence of an EPF system in mammals. Sera from 22 species were found

    to contain antigens that cross-reacted with mab against bovine EPF. They

    included 12 species of Bovidae, 4 of Cervidae, 1 Camelidae, 1 Suidae, 1

    Rhinoceroidae, 1 Tapiridae, and 2 Equidae. No cross-reactive antigens

    were found in 2 species of Felidae, 3 of Ursidae, 1 of Elephantidae, and 1

    of Hominidae. These results indicate the presence of the bovine

    EPF-active mol. in mammals other than Bovidae and support the assumption

    that EPF represents an early system in phylogenesis.
- L2 ANSWER 15 OF 32 CA COPYRIGHT 2003 ACS
- TI Bovine \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* : its characterization and an attempt to produce anti-bovine EPF \*\*\*antibody\*\*\*
- AB In a previous study, the authors suggested that bovine EPF had a mol. wt. of 21.5 kDa because a 21.5 kDa polypeptide was not found in the nonpregnant serum, and the isoelec. point was near 5.0 by 2D SDS-PAGE using non-equil. pH gradient electrophoresis. The authors extended the study to characterize the biochem. nature of purified bovine EPF. As a result, the isoelec. point of bovine EPF turned out to be 6.3 by 2D SDS-PAGE using isoelec. focusing. Also, the purified EPF was not reduced by the addn. of 2-mercaptoethanol, indicating that bovine EPF is a monomeric peptide. Amino acid anal. of EPF was attempted, but a definitive sequence could not be confirmed. In the present study, the crude anti-EPF IgG fraction was purified by adsorption with CNBr-activated Sepharose 4B coupled with nonpregnant bovine whole serum. The purified anti-EPF IgG decreased the rosette inhibition titer of pregnant serum from 6 to 3. The Sepharose 4B affinity column coupled with anti EPF-IgG effectively isolated the EPF from pregnant bovine serum.
- L2 ANSWER 16 OF 32 CA COPYRIGHT 2003 ACS
- TI Effect of monoclonal \*\*\*antibodies\*\*\* to \*\*\*early\*\*\*

  \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* (EPF) on the in vivo growth of transplantable murine tumors. [Erratum to document cited in CA116(23):233475n]
- AB Errors in Table 1 have been cor. The errors were not reflected in the abstr. or the index entries.
- L2 ANSWER 17 OF 32 CA COPYRIGHT 2003 ACS
- TI \*\*\*Early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* has immunosuppressive and growth factor properties
- AB A review with 49 refs. \*\*\*Early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\*

  (EPF) was first described as a pregnancy-assocd. substance, although recent studies suggest a more general link with cell development. It is a product of actively dividing cells, and its apparent functional importance to them suggests its potential as a regulator of cell proliferation. The recent discovery of EPF in platelets has provided a comparatively rich and readily available source of EPF. The purifn. procedures employed to isolate EPF from this source have also been applied to pregnancy serum and urine, medium conditioned by estrous mouse ovaries (stimulated with prolactin and embryo-conditioned medium), medium conditioned by tumor

cells, and serum from rats 24 h after partial hepatectomy (PH). instances, biol. activity followed the same pattern throughout. Furthermore, the final active reversed-phase high-performance liq. chromatog. fraction from all sources was bound specifically by immobilized anti-EPF monoclonal \*\*\*antibodies\*\*\* (MAbs), indicating that the active fractions produced from these diverse sources are very closely related, of not identical. Some differences have been obsd. in the behavior of EPF in various conditions. EPF is produced by proliferating tumor cells and by liver cells post-PH, and passive immunization studies with anti-EPF MAbs have shown that these cells need EPF for survival. contrast, EPF has not been detected as a product of the pre-embryo, and addn. of anti-EPF MAbs to embryo cultures does not adversely affect development from the 2-cell to the blastocyst stage. Although the pre-embryo is not dependent on EPF for its development in vitro, neutralization of EPF in vivo by anti-EPF MAbs retards its development. Thus, EPF appears to play an indirect role in maintaining the pre-embryo. By virtue of its ability to suppress the delayed-type hypersensitivity reaction, it has been suggested that EPF might act as an immunol. response modifier of the maternal immune system. Alternatively, the effect of EPF on lymphocytes may be to reduce the expression of all or some cytokines, and this could inhibit development. Whether or not EPF acts more directly as an autocrine growth factor from around the time of implantation, when the embryo first begins synthesis of EPF, is not known and remains to be investigated.

ANSWER 18 OF 32 CA COPYRIGHT 2003 ACS L2TIEffect of monoclonal \*\*\*antibodies\*\*\* to \*\*\*early\*\*\* \*\*\*factor\*\*\* (EPF) on the in vivo growth of \*\*\*pregnancy\*\*\* transplantable murine tumors AΒ Neutralization studies with monoclonal \*\*\*antibodies\*\*\* (mAbs) \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* have shown the factor to be essential for the continuation of pregnancy in mice and the growth of some tumor cells in vitro. These studies report that the mAbs are also able to limit the growth of 2 murine tumor lines transplanted s.c. The development of MCA-2 tumors in CBA mice was unaffected by the injection of 1 mg anti-EPF IgM at the time of tumor cell inoculation. However, 4 doses of 500 .mu.g anti-EPF, injected one dose per day for 4 days after tumor cell inoculation, retarded tumor development such that no tumors were palpable on day 13. A similar dose regimen of control IgM had no effect on tumor size. Dose/response studies revealed that lower doses of anti-EPF administered after tumor cell inoculation were effective in retarding the growth of the MCA-2 tumors. The effect of anti-EPF mAb administration on the growth rate of palpable B16 tumors established s.c. in C57BL/6 mice was also detd. injected with 6 mg anti-EPF 5/341 or anti-EPF 5/333 mAbs showed a decrease in the uptake of [3H] thymidine into tumor tissue, measured 16 h after injection. Furthermore, titrn. of sera for active EPF showed that a redn. in the EPF titer was assocd. with an inhibition of tumor DnA synthesis. Thus, it appears that neutralization of EPF retards tumor growth both in in vitro and in vivo. In vitro the effects must be due to anti-EPF mAb interfering with a direct mechanism that contributes to the maintenance of cells in the active growing phase. However, in vivo host immunol. mechanism that are modified to allow tumor survival may also be affected. The presence of EPF-induced suppressor factors circulating in the serum of

L2 ANSWER 19 OF 32 CA COPYRIGHT 2003 ACS

to tumor progression must now be investigated.

TI Relationship between \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\*, mouse embryo-conditioned medium and platelet-activating factor

AB The effects of synthetic platelet-activating factor (PAF-acether) and

mouse embryo-conditioned medium (a source of embryo-derived PAF (EPAF)) on prodn. of \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* (EPF) were

tumor-bearing mice has been confirmed and the contribution of such factors

compared. Embryo-conditioned medium, itself inactive in the EPF bioassay, stimulated ovarian prodn. of EPF in vitro but PAF-acether did not. vivo, embryo-conditioned medium induced EPF activity in serum of estrous female, but not in male and female mice. This PAF-induced activity was transitory, declining by 2 h and disappearing by 3 h after injection. Activity induced by embryo-conditioned medium was 1st evident at 2 h after injection, serum concns. increasing up to 6 h after injection. By discriminating between the behavior of PAF-acether and EPAF, these studies reinforce the conclusions of other workers that the mol. produced by the embryo is not PAF. Further investigations into the mechanism of action of PAF-acether revealed that it is a potent inducer of activity in the EPF bioassay, with an abs. requirement for platelets in the spleen cell suspension used in the assay. This platelet-derived active species was bound specifically by an anti-EPF monoclonal \*\*\*antibody\*\*\* indicating that it is EPF-like. This is consistent with parallel studies showing the platelets are not required for induction of activity by either pregnancy serum or purified EPF. These studies were applied to the PAF-induced leukotriene-like species, which had been found by others to be active in the EPF bioassay. Pregnancy serum induced the appearance of this substance from the spleen cell suspension used in the assay; thus the leukotriene-like substance may be regarded as an effector mol. in vitro or mediator of the initiating stimulus of EPF in the bioassay.

L2 ANSWER 20 OF 32 CA COPYRIGHT 2003 ACS

AB

- TI Identification of molecules involved in the ' \*\*\*early\*\*\*
  - \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* ' phenomenon

An isolated prepn. from ovine placental exts. which was active in the rosette inhibition assay mimicking the activity of the so-called \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* (EPF) has been shown t contain a 12 kDa polypeptide which could be partially resolved from low-mol.-wt. active moieties. N-Terminal amino acid sequence anal. of the polypeptide indicated that it was ovine thioredoxin, an identification confirmed by isolation and complete sequence anal. of the corresponding The cDNA for human thioredoxin was expressed in Escherichia coli and the recombinant protein isolated and purified. Pure recombinant thioredoxin alone did not induce the expression of increased rosette inhibition titers (RITs) when tested in the rosette inhibition assay; but, when tested in combination with cell stimuli such as platelet-activating factor (PAF) or serum, it allowed the expression of increased RITs where none was achieved in its absence. Thioredoxin acted in the assay to reverse a refractory state normally induced by these stimuli, allowing lipoxygenase-dependent moieties also induced by the stimuli to exert their effects, resulting in the expression of increased RITs.

\*\*\*Antibodies\*\*\* to recombinant thioredoxin removed from pregnancy sera the capacity to induce increased RITs, i.e. to express EPF activity, thus establishing a role for thioredoxin or thioredoxin-like proteins and assocd. mols. in the mechanisms which allow pregnancy sera to induce increased RITs. Based on a consideration of these and other results, a new model for the study of the EPF phenomenon is presented and discussed.

- L2 ANSWER 21 OF 32 CA COPYRIGHT 2003 ACS
- TI Bovine \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* (EPF) activity dependent on a 67-kDa polypeptide
- AB Maternal bovine EPF activity can be reduced to 1 single polypeptide enriched and identified from serum of cows in early pregnancy. The relative mol. wt. of this active polypeptide was 67 kDa. This bovine EPF was labeled by 125I and peroxidase. In parallel investigations of non-pregnant animals a 67-kDa polypeptide was addnl. identified in the last purifn. step, but without EPF activity in the rosette inhibition test. This indicated occurrence of an inactive precompound (or carrier protein) of the EPF in the non-pregnant state. On preincubation of lymphocytes with EPF analogs (inactive polypeptide from nonpregnancy serum) EPF retained its optimal activity, its lymphocyte receptors being

unaffected. Monoclonal \*\*\*antibodies\*\*\* produced against
HPLC-enriched EPF were reactive to the 67-kDa polypeptide in pregnancy
material as well as in nonpregnancy material and were not able to
differentiate between pregnant and nonpregnant. A mouse anti-EPF serum
produced against highly purified EPF isolated from SDS PAGE showed
reactivity only against the 67-kDa polypeptide of pregnancy serum but not
against that of non-pregnancy serum. This is the 1st evidence for a
difference in antigenic determinants of the two 67-kDa proteins found in
pregnancy and non-pregnancy serum. Furthermore, a 2nd higher mol. wt.
protein could be identified by this antiserum in pregnancy and
non-pregnancy serum.

L2ANSWER 22 OF 32 CA COPYRIGHT 2003 ACS \*\*\*Antibodies\*\*\* to \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* TI\*\*\*early\*\*\* retard embryonic development in mice in vivo Passive immunization of mice against \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* AΒ \*\*\*factor\*\*\* (EPF) leads to failure to maintain pregnancy. This treatment affects the development of the embryos very early in gestation. By Day 3, 54 and 25% of embryos treated with anti-EPF IgG and IgM, resp., had not developed to the 4-cell stage, compared with 12 and 1% in the control groups. None of the embryos in the mice treated with anti-EPF had developed beyond the 8-cell stage. A similar delay in the development after the treatment was obsd. on Day 4. The effect during the early stages of cleavage was indirect rather than direct, as 2-cell embryos (32-36 h post coitum) cultured in vitro in the presence of anti-EPF \*\*\*antibodies\*\*\* developed to the morula and blastocyst stage. delay in development did not appear to be caused by a disruption of the normal pattern of circulating progesterone, as progesterone concns. on Day 4 were within the normal range.

L2 ANSWER 23 OF 32 CA COPYRIGHT 2003 ACS
TI Monoclonal \*\*\*antibodies\*\*\* to \*\*\*early\*\*\* \*\*\*pregnancy\*\*\*

\*\*\*factor\*\*\* perturb tumor cell growth

\*\*\*early\*\*\* \*\*\*pregnancy\*\*\* The pregnancy-assocd. substance \*\*\*factor\*\*\* (EPF) has previously been reported as a product of tumors of germ cell origin. More recently EPF (or an EPF-related substance, tEPF) has also been detected in the serum of patients bering tumors of non-germ cell origin. Here, the prodn. is reported of tEPF by a variety of cultured transformed and tumor cell lines, of both germ and non-germ \*\*\*Antibodies\*\*\* specific for EPF remove all tEPF cell origin. activity from tumor cell conditioned medium. TEPF prodn. is assocd. with cell division; tEPF is no longer detected after growth arrest or differentiation. Co-culture of tumor cells with increasing doses of anti-EPF monoclonal \*\*\*antibodies\*\*\* resulted in a significant, dose-dependent decrease in rate of growth and viability. Similar anti-EPF concns. have no effect on the ConA-induced proliferation of mouse spleen Thus, tEPF is a growth-regulated product of cultured tumor and transformed cells. These cells are also dependent upon tEPF for continued growth, i.e. tEPF is acting in the autocrine mode.

L2 ANSWER 24 OF 32 CA COPYRIGHT 2003 ACS

AB

TI Methods, \*\*\*antibodies\*\*\* , and kits for immunochemical determination of normal or abnormal pregnancy

AB Methods, (un)labeled polyclonal and monoclonal \*\*\*antibody\*\*\*
reagents, and kits are provided for the detection of normal or ectopic
pregnancy, ex vivo products of conception, or increased risk of preterm
labor and membrane rupture. Individual methods rely on the detn. of an
unrestricted pregnancy antigen or the presence or absence of a fetal
restricted antigen in a sample taken from the cervical canal, cervical os,
or posterior fornix, or a sample expelled or removed from the uterus.
Immunoassay procedures for the above detns. are described. The pregnancy
antigen may be human chorionic gonadotropin, somatostatin,
.alpha.-fetoprotein, etc. Pregnancy can be detd. in the 1st trimester or

in the 1st 20 wk. Swab samples collected in the vicinity of the cervical os were immersed in a diluent contg. 0.05M Tris-HCl (pH 7.4), 0.15M NaCl, 0.02% NaN3, 1% bovine serum albumin, 500 kallikrein units/mL aprotinin, 1 mM phenylmethylsulfonyl fluoride, and 5 mM EDTA. Microtiter plate wells were reacted 1st with goat F(ab')2 anti-mouse IgG \*\*\*antibody\*\*\* with mouse monoclonal anti-(fetal fibronectin) ascites (prodn. and purifn. of monoclonal \*\*\*antibody\*\*\* given). A 100 .mu.L portion of each sample, std., pos. control (amniotic fluid of known fibronectin concn.), and neg. control (sample diluent) was placed in sep. wells and incubated for 2 h at room temp. Following washing, each well was further incubated with alk. phosphatase-conjugated goat anti-human fibronectin, then with enzyme substrate; developed color was read at 405 nm. A std. curve was constructed by correlating increasing reaction rate with increasing fibronectin concn. in the stds. Samples obtained before wk 20 of pregnancy which demonstrate significant fetal fibronectin in the test sample indicate normal uterine pregnancy; samples in which significant amts. of fetal fibronectin are absent indicate that normal uterine pregnancy is not present.

- L2ANSWER 25 OF 32 CA COPYRIGHT 2003 ACS TI\*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* pregnant and nonpregnant subjects with the rosette inhibition test The authors tested for \*\*\*early\*\*\* AΒ \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* (EPF) using a rosette inhibition test with polyclonal anti-lymphocyte serum from the horse and 2 monoclonal \*\*\*antibodies\*\*\* specific for the E-receptor of T-lymphocytes. When lymphocytes were preincubated with early human pregnancy sera, rosette inhibition titers were 4 or more dilns. higher than when lymphocytes were preincubated with nonpregnant sera.
- L2ANSWER 26 OF 32 CA COPYRIGHT 2003 ACS TI Passive immunization of pregnant mice against \*\*\*early\*\*\* \*\*\*factor\*\*\* causes loss of embryonic viability pregnancy\*\*\* \*\*\*factor\*\*\* (EPF) is a monitor \*\*\*pregnancy\*\*\* \*\*\*Early\*\*\* \*\*\*pregnancy\*\*\* AB (EPF) is a monitor of the incidence of fertilization and the progress of the early embryo. det. whether, as well as being a marker of embryonic viability, EPF is also necessary for embryonic survival, passive immunization studies with monoclonal and polyclonal \*\*\*antibodies\*\*\* to EPF were carried out on pregnant mice. In the prepn. of monoclonal \*\*\*antibodies\*\*\* noted that most anti-EPF producing hybridomas failed to grow in vitro, while those that did grow produced only low yields of specific IgM \*\*\*antibodies\*\*\* . Two stable hybridoma cell lines were established bot producing low affinity anti-EPF IgM; polyclonal anti-EPF IgG was prepd. in rabbits. Mice were passively immunized with 500 .mu.q monoclonal anti-EPF IgM at 32 and 56 h post coitum (total dose 1 mg) or with 500 .mu.g monoclonal anti-EPF IgG at 8, 16, 32, and 40 h post column (total dose 2 mg). At 10 days, only 6/18 and 3/6 mice receiving monoclonal
  - \*\*\*antibodies\*\*\* and 2/7 and 1/6 mice receiving polyclonal
    \*\*\*antibodies\*\*\* had maintained their pregnancies. In contrast, all
    mice receiving control IgM or control IgM and 22/23 receiving saline were
    still pregnant at day 10.
- L2 ANSWER 27 OF 32 CA COPYRIGHT 2003 ACS
  TI Neoplasm diagnosis and treatment, and pregnancy testing and termination, using \*\*\*antibodies\*\*\* to \*\*\*early\*\*\* \*\*\*pregnancy\*\*\*

sing \*\*\*antibodies\*\*\* to \*\*\*early\*\*\* \*\*\*pregnancy\*\*\*
\*\*\*factor\*\*\* (EPF)

AB Monoclonal and polyclonal \*\*\*antibodies\*\*\* , and active fragments thereof, to EPF can be used to identify tumor cells which produce EPF, for diagnosis and treatment of cancer, for detection of EPF in the serum during pregnancy, and for diagnosis and termination of pregnancy in mammals. Treatment of mouse fibrosarcoma MCA2 cells in vitro with monoclonal anti-EPF \*\*\*antibody\*\*\* 7/342 (.gtoreq.0.16 .mu.M) resulted in cell detachment, clumping, and killing. Mice inoculated with MCA2

cells and then treated with  $500 \, .mu.g \, 7/342$  daily for 4 days did not develop tumors.

- L2 ANSWER 28 OF 32 CA COPYRIGHT 2003 ACS
- TI \*\*\*Early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* : large scale isolation of rosette inhibition test-active polypeptides from ovine placental extracts
- AB Protocols are described for the isolation of substantial (mg) amts. of a rosette inhibition test (RIT)-active polypeptide fraction from ovine The main component of the prepn. is a 12-kilodalton (K) placental exts. polypeptide which contains a highly reactive thiol group. Oxidn. may occur during isolation with the result that the final prepn. is a mixt. of the 12K polypeptide and a 25K disulfide linked dimer. The highly reactive thiol group was directly involved in activity expression, since gentle redn. followed by iodoacetylation resulted in a complete loss of activity. \*\*\*antibodies\*\*\* removed all the RIT Antisera were prepd. and the activity from fresh ovine placental exts., indicating that mols. related to those in the isolated prepn. were responsible for all the activity in crude exts. The \*\*\*antibodies\*\*\* also removed all the RIT activity from ovine and murine pregnancy sera, obtained both before and after \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* implantation. Since (EPF) is defined as an RIT activity detected in pregnancy serum, these results establish that EPF activity is due to mols. similar to those isolated from the placental exts. The availability of the preparative protocol and \*\*\*antibodies\*\*\* should hasten the biochem. definition of the EPF phenomenon.
- L2 ANSWER 29 OF 32 CA COPYRIGHT 2003 ACS
- TI Detecting \*\*\*early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* (EPF) in mammals, purifying EPF and method for producing a monoclonal \*\*\*antibody\*\*\*
- AΒ Cells which produce EPF are grown in a culture medium to produce a supernatant medium contg. the EPF. To purify the EPF, the EPF is absorbed by a selective absorbent in a column, dialyzed against a buffer soln., concd. and gel-filtered. Selected fractions of the filtrate undergo reversed-phase HPLC, and the purified EPF is eluted from the chromatog. column. Monoclonal \*\*\*antibodies\*\*\* to EPF are produced to detect the presence of EPF in serum and to provide a means for detecting pregnancy in female mammals. An early pregnancy test kit is described. EPF is purified from human choriocarcinoima, myeloma, and lymphoblastic leukemic cells by immunoadsorption using goat/anti-mouse EPF on CNBr-activated Sepharose 4B, gel filtration on Sephacryl S-200, and reversed-phase HPLC on Beckman RPSC ultrapore. Spleen-myeloma hybrid cells from mice immunized with human EPF are selected for anti-EPF formation and cloned for monoclonal \*\*\*antibody\*\*\* manuf.
- L2 ANSWER 30 OF 32 CA COPYRIGHT 2003 ACS
- TI Improvement of the rosette inhibition test including some remarks on the possible mechanism of EPF in the RIT
- The rosette inhibition test (RIF) for the detn. of \*\*\*early\*\*\*

  \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* (EPF) in human serum or urine was modified. The monoclonal \*\*\*antibody\*\*\* anti-HuLyl-3 was used in place of anti-lymphocyte sera, and rosette formation was evaluated after lymphocyte nuclei were stained with acridine orange. SEM studies did not show any differences in the surface charge of lymphocytes preincubated with control or pregnancy serum. However, transmission electron microscopic results did suggest a difference in surface charge and verified the general neg. charge of the lymphocyte surface.
- L2 ANSWER 31 OF 32 CA COPYRIGHT 2003 ACS
- TI \*\*\*Early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* of human urine
  AB \*\*\*Early\*\*\* \*\*\*pregnancy\*\*\* \*\*\*factor\*\*\* (EPF) from urine of
  women .ltoreq.28 wk pregnant was dialyzed and serially ultrafiltrated.

EPF was detected in the >50,000-dalton and 3500-10,000-dalton fractions. The low-mol.-wt.-fraction EPF was dialyzable, but when mixed with the 10,000-25,000-dalton fraction became nondialyzable. Thus, in pregnant urine EPF exists as a low-mol.-wt. entity bound to a larger carrier. Polyclonal antisera and monoclonal \*\*\*antibodies\*\*\* to EPF were prepd. and characterized.

L2ANSWER 32 OF 32 CA COPYRIGHT 2003 ACS Purification and partial characterization of EPF TI\*\*\*Early\*\*\* ABfrom the conditioned medium from the human choriocarcinoma cell line BeWo by immunoabsorption, gel filtration, and reverse-phase HPLC. Approx. 50 .mu.g EPF was obtained from 2 L of conditioned medium, and an overall purifn. factor of 2 .times. 105 was achieved. The human tumor EPF, which is a postimplantation EPF, consisted of a single peptide of 16,000 mol. wt. In spite of numerous differences between the human tumor EPF and that previously purified from mouse ovaries and oviducts, the human and mouse EPF were immunol. similar. Both exerted an inhibition of rosette formation, indicating the stimulation of release of lymphocyte suppressor factors. Also, the \*\*\*antibodies\*\*\* to mouse EPF bound to human EPF. In addn. to the above data, a review of the purifn. and properties of mouse ovary and oviduct EPF is given. => d all 7 13 14 29 L2ANSWER 7 OF 32 CA COPYRIGHT 2003 ACS AN131:127375 CA TIMethod and apparatus for detecting conception in animals using \*\*\*antibodies\*\*\* to \*\*\*early\*\*\* \*\*\*conception\*\*\* \*\*\*factor\*\*\* INJordan, Nancy Tommye; Jordan, John Douglas Concepto Diagnostics, USA PASO PCT Int. Appl., 24 pp. CODEN: PIXXD2 DTPatent LA English IC ICM G01N033-543 CC9-1 (Biochemical Methods) Section cross-reference(s): 13, 15 FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. --**-**-----------A1 19990805 WO 1999-US2331 19990202 PIWO 9939208 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,

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KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
            MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2319417
                      AA
                           19990805
                                        CA 1999-2319417 19990202
    AU 9925795
                      A1
                           19990816
                                         AU 1999-25795
                                                           19990202
    EP 1053473
                      A1
                           20001122
                                          EP 1999-905689
                                                          19990202
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
    BR 9908550
                      Α
                           20001128
                                          BR 1999-8550
                                                           19990202
     JP 2002502036
                      T2
                           20020122
                                          JP 2000-529611
                                                           19990202
    US 2001024799
                      A1
                           20010927
                                          US 2001-764826
                                                           20010117
PRAI US 1998-16995
                     Α
                           19980202
                    W
    WO 1999-US2331
                           19990202
    The present invention provides ***antibodies*** which specifically
AΒ
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bind ***early*** ***conception*** ***factor***
                                                             , which can be
     found in body fluids of animals including but not limited to the cow, cat,
     dog, horse, human, sheep, and pig. The invention provides methods for
     detecting conception or the absence of conception in an animal, the latter
    being recognized by the absence of ***early***
                                                        ***conception***
                    in a suitable body fluid collected from the animal.
       ***factor***
    Apparatus for detecting ***early***
                                            ***conception***
       ***factor***
                     in a body fluid from an animal comprising the
       ***antibodies***
                        which specifically bind ***early***
       ***conception***
                           ***factor*** are also provided.
ST
      ***early***
                     ***conception***
                                         ***factor***
                                                           ***antibody***
    app fertilization
IT
     Immunoglobulins
    RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BPR
     (Biological process); BSU (Biological study, unclassified); PRP
     (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
                                       ***conception***
        (A, monoclonal, to
                          ***early***
        ; method and app. for detecting conception in animals using
         ***antibodies*** to ***early*** ***conception***
         ***factor***
IT
    Glycoproteins, specific or class
    RL: ANT (Analyte); BPR (Biological process); BSU (Biological study,
    unclassified); BUU (Biological use, unclassified); PUR (Purification or
    recovery); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
                                               ***factor*** ); method
        (ECF ( ***early***
                             ***conception***
       and app. for detecting conception in animals using ***antibodies***
            ***early***
                           ***conception***
                                                ***factor*** )
IT
    Immunoassay
        (app.; method and app. for detecting conception in animals using
         ***antibodies*** to ***early***
                                              ***conception***
         ***factor***
IT
     Insemination, artificial
        (assay for ***early*** ***conception***
                                                       ***factor***
       humans and cows in relation to; method and app. for detecting
       conception in animals using ***antibodies*** to ***early***
         ***conception***
                           ***factor*** )
IT
      ***Antibodies***
    RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical
    study); BIOL (Biological study); PROC (Process); USES (Uses)
                     ***early***
                                     ***conception***
                                                           ***factor*** ;
        (chimeric, to
       method and app. for detecting conception in animals using
         ***antibodies***
                          to ***early***
                                              ***conception***
         ***factor***
IT
      ***Antibodies***
    RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical
    study); BIOL (Biological study); PROC (Process); USES (Uses)
        (conjugates, to ***early***
                                      ***conception***
                                                             ***factor***
       with detectable group; method and app. for detecting conception in
       animals using ***antibodies*** to ***early***
         IT
    Blood analysis
    Blood serum
    Body fluid
    Milk analysis
    Urine analysis
       ( ***early***
                         ***conception***
                                             ***factor***
                                                             detection in;
       method and app. for detecting conception in animals using
         ***antibodies*** to ***early***
                                                ***conception***
         ***factor*** )
```

```
IT
    Cat (Felis catus)
     Cattle
     Dog (Canis familiaris)
     Horse (Equus caballus)
     Swine
          ***early***
                          ***conception***
                                              ***factor***
                                                             of; method and
        app. for detecting conception in animals using ***antibodies***
          ***early***
                        ***conception***
                                              ***factor*** )
ΙT
    Hybridoma
                         ***antibody***
        (for monoclonal
                                          prodn.; method and app. for
        detecting conception in animals using ***antibodies***
         ***early***
                        ***conception***
                                              ***factor***
IT
       ***Antibodies***
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical
     study); BIOL (Biological study); PROC (Process); USES (Uses)
        (humanized, to ***early*** ***conception***
                                                             ***factor*** ;
        method and app. for detecting conception in animals using
         ***antibodies***
                           ***conception***
         ***factor***
IT
       ***Antibodies***
     RL: ARG (Analytical reagent use); DEV (Device component use); SPN
     (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (immobilized, to ***early***
                                        ***conception***
                                                               ***factor***
       method and app. for detecting conception in animals using
         ***antibodies***
                           ***conception***
         ***factor*** )
ΙT
    Animal
    Fertilization
     Immunoassay
        (method and app. for detecting conception in animals using
         ***antibodies***
                          to ***early*** ***conception***
         ***factor***
IT
       ***Antibodies***
    RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU
     (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (monoclonal, conjugates, to ***early***
                                                     ***conception***
         ***factor***
                       , with colloidal gold; method and app. for detecting
        conception in animals using
                                   ***antibodies*** to ***early***
                              ***factor*** )
         ***conception***
IT
      ***Antibodies***
    RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BPR
     (Biological process); BSU (Biological study, unclassified); PRP
     (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
        (monoclonal, to
                        ***early***
                                         ***conception***
                                                             ***factor*** ;
       method and app. for detecting conception in animals using
         ***antibodies***
                                ***early***
                           to
                                              ***conception***
         ***factor***
IT
    Membranes, nonbiological
        (nitrocellulose, with immobilized ***antibodies***
                                                             to
                              ***factor*** ; method and app. for detecting
         ***conception***
       conception in animals using ***antibodies*** to ***early***
         ***conception***
                             ***factor*** )
IT
      ***Antibodies***
    RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BPR
     (Biological process); BSU (Biological study, unclassified); THU
     (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP
     (Preparation); PROC (Process); USES (Uses)
             ***early***
                             ***conception***
                                                 ***factor*** ; method and
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app. for detecting conception in animals using ***antibodies***
                                                                       to
                       ***conception*** ***factor*** )
         ***early***
     7440-57-5D, Gold, conjugates with ***antibody*** to ***conception*** ***factor*** , biological studies
IT
                                                           ***earlv***
     RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (colloidal; method and app. for detecting conception in animals using
         ***antibodies*** to ***early*** ***conception***
         ***factor***
     9003-99-0D, Peroxidase, conjugates with ***antibody***
ΙT
                     ***conception*** ***factor***
       ***early***
     RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (horseradish; method and app. for detecting conception in animals using
         ***antibodies*** to ***early*** ***conception***
         ***factor***
IT
     9004-70-0D, Nitrocellulose, with immobilized anti- ***early***
      RL: DEV (Device component use); USES (Uses)
        (membrane; method and app. for detecting conception in animals using
         ***antibodies*** to ***early*** ***conception***
         ***factor***
IT
     9001-78-9D, conjugates with ***antibody*** to ***early***
      RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (method and app. for detecting conception in animals using
         ***antibodies*** to ***early*** ***conception***
         ***factor*** )
RE.CNT
             THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) May; US 5602040 A 1997 CA
(2) Quinn, K; Cancer Immunology Immunotherapy 1992, V34, P265 CA
L2
    ANSWER 13 OF 32 CA COPYRIGHT 2003 ACS
AN
    121:26964 CA
ΤI
    Study of ***early***
                              ***pregnancy*** ***factor*** (EPF). 2
    Ito, Kazue; Yasuda, Yasuhisa
ΑU
    Akita Prefect. Coll. Agric., Akita, 010-04, Japan
CS
    Chikusan no Kenkyu (1994), 48(5), 555-8
SO
    CODEN: CKNKAJ; ISSN: 0009-3874
DT
    Journal; General Review
LA
    Japanese
CC
    2-0 (Mammalian Hormones)
AΒ
    A review, with 117 refs., on the prepn. of polyclonal and monoclonal
      ***antibodies*** specific for EPF for EIA, and hypotheses on the prodn.
               early*** ***pregnancy*** ***factor***

***antibody*** ***early***
    and action mechanism of EPF.
ST
    review
           ***early***
    mechanism;
                                                ***pregnancy***
      ***factor*** prepn review
      ***Antibodies***
IT
    RL: SPN (Synthetic preparation); PREP (Preparation)
            ***early*** ***pregnancy*** ***factor*** , prepn. of)
IT
    Glycoproteins, specific or class
    RL: SPN (Synthetic preparation); PREP (Preparation)
       ***antibody*** prepn. for and action mechanism of)
L2
    ANSWER 14 OF 32 CA COPYRIGHT 2003 ACS
AN
    120:319891 CA
ΤI
    Detection of bovine ***early*** ***pregnancy***
                                                           ***factor***
    (EPF) active polypeptide in different species of mammals
```

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Klima, F.; Schadow, D.; Schroder, H. -D.; Pitra, Ch.
AU Î
    Inst. Zoo and Wild Anim. Res., Berlin, Germany
CS
    EOS--Rivista di Immunologia ed Immunofarmacologia (1993), 13(3-4), 189-92
SO
    CODEN: EOSSDJ; ISSN: 0392-6699
DT
    Journal
LA
    English
CC
    13-1 (Mammalian Biochemistry)
    The authors studied the cross-reactivity between bovine ***early***
AB
      females of 47 species by a monoclonal ***antibody*** (mab) capable of
    recognizing the EPF-active polypeptide in cattle to obtain data on the
    occurrence of an EPF system in mammals. Sera from 22 species were found
    to contain antigens that cross-reacted with mab against bovine EPF. They
    included 12 species of Bovidae, 4 of Cervidae, 1 Camelidae, 1 Suidae, 1
    Rhinoceroidae, 1 Tapiridae, and 2 Equidae. No cross-reactive antigens
    were found in 2 species of Felidae, 3 of Ursidae, 1 of Elephantidae, and 1
    of Hominidae. These results indicate the presence of the bovine
    EPF-active mol. in mammals other than Bovidae and support the assumption
    that EPF represents an early system in phylogenesis.
ST
      ***early***
                   ***pregnancy***
                                       ***factor***
IT
    Mammal
                       ***pregnancy*** ***factors*** of)
        ( ***early***
    Glycoproteins, specific or class
IT
    RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
    BIOL (Biological study); OCCU (Occurrence)
          L2
    ANSWER 29 OF 32 CA COPYRIGHT 2003 ACS
ΑN
    107:20377 CA
              ΤI
    Detecting
    mammals, purifying EPF and method for producing a monoclonal
      ***antibody***
IN
    Morton, Halle; Cavanagh, Alice Christina; Rolfe, Barbara Ellen
PA
    University of Queensland, Australia
SO
    PCT Int. Appl., 21 pp.
    CODEN: PIXXD2
DT
    Patent
LA
IC
    C07K015-06; C07K015-12; C07K003-20; C12N015-00
CC
    9-3 (Biochemical Methods)
    Section cross-reference(s): 15
FAN.CNT 1
    PATENT NO. KIND DATE
                                 APPLICATION NO. DATE
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                                       -----
    WO 8605498 A1
PΙ
                          19860925
                                       WO 1986-AU60
                                                       19860312
        W: AU, GB, JP, US
        RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE
    AU 8655897 A1 19861013 AU 1986-55897

AU 599021 B2 19900712

JP 62502304 T2 19870910 JP 1986-501847

GB 2192634 A1 19880120 GB 1987-20636

GB 2192634 B2 19900321

EP 262119 A1 19880406 EP 1986-901744
                                                         19860312
                                                         19860312
                                                        19860312
                                       EP 1986-901744
                                                         19860312
        R: AT, BE, CH, DE, FR, IT, LI, NL, SE
PRAI AU 1985-9664
                         19850312
    AU 1985-9750
                          19850315
    AU 1985-2402
                          19850912
    WO 1986-AU60
                          19860312
AΒ
    Cells which produce EPF are grown in a culture medium to produce a
    supernatant medium contg. the EPF. To purify the EPF, the EPF is absorbed
    by a selective absorbent in a column, dialyzed against a buffer soln.,
    concd. and gel-filtered. Selected fractions of the filtrate undergo
    reversed-phase HPLC, and the purified EPF is eluted from the chromatog.
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column. Monoclonal ***antibodies*** to EPF are produced to detect the
    presence of EPF in serum and to provide a means for detecting pregnancy in
    female mammals. An early pregnancy test kit is described. EPF is
    purified from human choriocarcinoima, myeloma, and lymphoblastic leukemic
    cells by immunoadsorption using goat/anti-mouse EPF on CNBr-activated
    Sepharose 4B, gel filtration on Sephacryl S-200, and reversed-phase HPLC
    on Beckman RPSC ultrapore. Spleen-myeloma hybrid cells from mice
    immunized with human EPF are selected for anti-EPF formation and cloned
    for monoclonal ***antibody*** manuf.
ST
      ***early***
                    ***pregnancy***
                                       ***factor*** human monoclonal
      ***antibody***
    Pregnancy
IT
       (detection of, ***early*** ***pregnancy*** ***factor***
       purifn. and monoclonal ***antibody*** prepn. for)
IT
    Blood analysis
    Urine analysis
       immunoassay)
IT
    Myeloma
       ( ***early*** ***pregnancy*** ***factor*** of, of human purifn. of and prepn. of monoclonal ***antibodies*** to, for
                                         ***factor*** of, of human,
       pregnancy detection)
IT
    Carcinoma
       (chorio-, ***early*** ***pregnancy*** ***factor*** of, of
       human, purifn. of and prepn. of monoclonal ***antibodies*** to, for
       pregnancy detection)
IT
    Proteins, specific or class
    RL: SPN (Synthetic preparation); PREP (Preparation)
          prepn. of monoclonal ***antibodies*** to, for pregnancy detection)
IT
    Leukemia
                                                      ***factor***
       (lymphoblastic, ***early*** ***pregnancy***
       of, of human, purifn. of and prepn. of monoclonal ***antibodies***
       to, for pregnancy detection)
      ***Antibodies***
IT
    RL: SPN (Synthetic preparation); PREP (Preparation)
       (monoclonal, to ***early*** ***pregnancy*** ***factor*** ,
       prepn. and use of, for pregnancy detection)
=> d his
    (FILE 'HOME' ENTERED AT 18:59:48 ON 09 MAY 2003)
    FILE 'CA' ENTERED AT 19:00:02 ON 09 MAY 2003
L1
          132 S (EARLY PREGNANCY FACTOR?) OR (EARLY CONCEPTION FACTOR?)
L2
           32 S L1 AND ANTIBOD?
=> s 12 and urine
       187346 URINE
L3
           7 L2 AND URINE
=> d ti 1-7
L3
    ANSWER 1 OF 7 CA COPYRIGHT 2003 ACS
TI
    Bovine pregnancy test
L3
    ANSWER 2 OF 7 CA COPYRIGHT 2003 ACS
    Method and apparatus for detecting conception in animals using
      ***antibodies*** to ***early*** ***conception***
                                                            ***factor***
    ANSWER 3 OF 7 CA COPYRIGHT 2003 ACS
L3
      ΤI
```

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ANSWER 4 OF 7 CA COPYRIGHT 2003 ACS
L3
TI
    Neoplasm diagnosis and treatment, and pregnancy testing and termination,
          ***antibodies*** to ***early*** ***pregnancy***
      ***factor***
                   (EPF)
    ANSWER 5 OF 7 CA COPYRIGHT 2003 ACS
L3
ΤI
    Detecting
              (EPF) in
    mammals, purifying EPF and method for producing a monoclonal
      ***antibody***
    ANSWER 6 OF 7 CA COPYRIGHT 2003 ACS
L3
ΤI
    Improvement of the rosette inhibition test including some remarks on the
    possible mechanism of EPF in the RIT
    ANSWER 7 OF 7
                 CA COPYRIGHT 2003 ACS
L3
      ***Early***
                     ***pregnancy*** ***factor*** of human
TI
      ***urine***
=> d ab 7
L3
    ANSWER 7 OF 7 CA COPYRIGHT 2003 ACS
                     ***pregnancy*** ***factor*** (EPF) from
AΒ
      ***Early***
      ***urine***
                   of women .ltoreq.28 wk pregnant was dialyzed and serially
    ultrafiltrated. EPF was detected in the >50,000-dalton and
    3500-10,000-dalton fractions. The low-mol.-wt.-fraction EPF was
    dialyzable, but when mixed with the 10,000-25,000-dalton fraction became
                   Thus, in pregnant ***urine*** EPF exists as a
    nondialyzable.
    low-mol.-wt. entity bound to a larger carrier. Polyclonal antisera and
    monoclonal
                ***antibodies*** to EPF were prepd. and characterized.
=> d all 7
    ANSWER 7 OF 7 CA COPYRIGHT 2003 ACS
L3
AN
    105:112770 CA
TI
      ***Early***
                     ***urine***
AU
    Roberts, T. K.; Price, R.; Smart, Y. C.; Stevenson, K.; Tasevski, V.
CS
    Univ. Newcastle, 2308, Australia
SO
    Reproductive and Perinatal Medicine (1985), 1(Early Pregnancy Factors),
    191-3
    CODEN: RPMDER; ISSN: 0890-9989
DT
    Journal
LA
    English
CC
    13-6 (Mammalian Biochemistry)
    Section cross-reference(s): 9
                     ***preqnancy***
                                      ***factor*** (EPF) from
AΒ
      ***Early***
      ***urine*** of women .ltoreq.28 wk pregnant was dialyzed and serially
    ultrafiltrated. EPF was detected in the >50,000-dalton and
    3500-10,000-dalton fractions. The low-mol.-wt.-fraction EPF was
    dialyzable, but when mixed with the 10,000-25,000-dalton fraction became
    nondialyzable. Thus, in pregnant
                                    ***urine*** EPF exists as a
    low-mol.-wt. entity bound to a larger carrier. Polyclonal antisera and
                ***antibodies*** to EPF were prepd. and characterized.
    monoclonal
ST
      ***early***
                     ***pregnancy***
                                       ***factor***
                                                       ***urine***
    antiserum ***early***
                          ***preqnancy***
                                               ***factor***
                                     ***early***
      ***urine*** ; ***antibody***
                                                     ***pregnancy***
                    ***urine***
      ***factor***
IT
    Pregnancy
       ***urine***
```

and growth factor properties

```
of women in, characterization of)
IT
       ***Urine***
        characterization of)
IT
        (to ***early*** ***pregnancy***
                                                ***factor***
                                                                of
         ***urine*** of women, characterization of)
IT
     Proteins
    RL: PROC (Process)
                          ***pregnancy*** ***factors*** , of
        ( ***early***
         ***urine***
                       of women, characterization of)
IT
       ***Antibodies***
    RL: PROC (Process)
        (monoclonal, to ***early*** ***pregnancy***
                                                            ***factor***
                                                                            of
         ***urine*** of women, characterization of)
=> s 12 and milk
       125255 MILK
L4
            2 L2 AND MILK
=> d all 1-2
L4
    ANSWER 1 OF 2 CA COPYRIGHT 2003 ACS
AN
    138:300179 CA
ΤI
    Bovine pregnancy test
    Roth, J. W.; Colgin, Mark; Hurst, Roger; Newman, Diane; Landmann, Cathy
IN
PA
    U.S. Pat. Appl. Publ., 22 pp.
SO
    CODEN: USXXCO
DT
    Patent
LA
    English
IC
     ICM G01N033-53
     ICS C12M001-34; A01K067-027
NCL
     436510000; 435287200; 800015000
CC
     9-16 (Biochemical Methods)
     Section cross-reference(s): 2, 13, 15
FAN.CNT 1
    PATENT NO. KIND DATE
                                          APPLICATION NO. DATE
                    ----
                                          -----
    US 2003073248 A1 20030417
PI
                                          US 2002-255162 20020924
PRAI US 2001-325663P P
                          20010928
    US 2001-337871P P
                          20011108
    US 2002-377165P P
                         20020502
20020502
    US 2002-377166P P
    US 2002-377355P P 20020502
US 2002-377829P P 20020502
US 2002-377921P P 20020502
    US 2002-377987P P
                          20020502
    US 2002-380042P P 20020502
US 2002-380043P P 20020502
    This invention provides bovine pregnancy test methods and devices.
AΒ
                                                                        The
    test is also suitable for other ruminant and/or ungulate animals.
    Antigens from Group A (early pregnancy antigens), and/or Group B
     (mid-pregnancy antigens), and Group C (early, mid- and late pregnancy
    antigens) are detected in a fluid from the animal, and pregnancy is
    reliably detd. The pregnancy assays of this invention are preferably
    carried out using immunoassay devices which provide immediate results in
    the field.
ST
    cattle pregnancy test
IT
    Antigens
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
```

```
(1-8D; bovine pregnancy test)
IT
    Estrus
        (Behavioral; bovine pregnancy test)
IT
    Glycoproteins
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Bovine antigen; bovine pregnancy test)
IT
     Chemokines
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (C-X-C, GCP-2 (granulocyte chemotactic protein 2); bovine pregnancy
        test)
IT
    Containers
        (Cassette; bovine pregnancy test)
IT
        (Female; bovine pregnancy test)
    Antigens
IT
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Group A (early pregnancy); bovine pregnancy test)
IT
    Antigens
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Group B (mid-pregnancy); bovine pregnancy test)
IT
    Antigens
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Group C (early, mid-and late pregnancy); bovine pregnancy test)
    Antigens
IT
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (I-8U; bovine pregnancy test)
IT
    Transcription factors
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (IRF-2 (interferon regulatory factor 2); bovine pregnancy test)
    Proteins
IT
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (ISG17; bovine pregnancy test)
IT
    Transcription factors
    RL: ANT (Analyte); ANST (Analytical study)
        (ISGF-2 (interferon-stimulated gene factor 2); bovine pregnancy test)
IT
    Antigens
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Leu-13/9-27; bovine pregnancy test)
IT
     Proteins
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Mx; bovine pregnancy test)
IT
     Proteins
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Pregnancy serum protein 60; bovine pregnancy test)
IT
    Glycoproteins
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Pregnancy-assocd., PAG-1; bovine pregnancy test)
IT
    Glycoproteins
    RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Pregnancy-assocd., PAG-4; bovine pregnancy test)
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IT
    Glycoproteins
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Pregnancy-assocd., PAG-5; bovine pregnancy test)
     Glycoproteins
IT
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Pregnancy-assocd., PAG-6; bovine pregnancy test)
IT
     Glycoproteins
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Pregnancy-assocd., PAG-7; bovine pregnancy test)
     Glycoproteins
IT
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Pregnancy-assocd., PAG-9; bovine pregnancy test)
IT
     Proteins
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (Pregnancy-specific protein B; bovine pregnancy test)
IT
     Analytical apparatus
        (Test strip; bovine pregnancy test)
ΙT
     Immunoassay
        (app.; bovine pregnancy test)
IT
     Alces alces
     Alpaca (animal)
     Animal
     Animal cell
     Antelope
     Bison
     Blood analysis
     Blood plasma
     Blood serum
     Body fluid
     Bos grunniens
     Breeding, animal
     Buffalo
     Camel (Camelus bactrianus)
     Camel (Camelus dromedarius)
     Caribou and Reindeer (Rangifer)
     Cattle
     Containers
     Cytolysis
    Dairy cattle
    Elk
    Filters
    Gazelle
    Giraffa camelopardalis
    Goat
    Horse (Equus caballus)
     Immobilization, molecular
     Immunoassay
    Labels
    Lama glama
        ***Milk***
                      analysis
    Ovarian cycle
    Ovis canadensis
    Pregnancy
    Ruminant
    Saliva
    Sheep
    Swine
    Test kits
```

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Ungulate
     Urine analysis
     Vicugna vicugna
        (bovine pregnancy test)
IT
       ***Antibodies***
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (bovine pregnancy test)
IT
     Proteins
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
                          ***pregnancy*** ***factors***; bovine
        ( ***early***
        pregnancy test)
IT
     Temperature effects, biological
        (heat; bovine pregnancy test)
IT
       ***Antibodies***
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (monoclonal; bovine pregnancy test)
IT
     Eye
     Nose
     Vagina
        (secretions; bovine pregnancy test)
IT
     Microglobulins
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (.beta.2-; bovine pregnancy test)
IT
     57-83-0, Progesterone, analysis
                                      69106-44-1, 2',5' Oligoadenylate
                 329900-75-6, COX-2
     synthetase
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (bovine pregnancy test)
L4
     ANSWER 2 OF 2 CA COPYRIGHT 2003 ACS
AN
     131:127375
                CA
TI
     Method and apparatus for detecting conception in animals using
       ***antibodies***
                        to
                              ***factor***
IN
     Jordan, Nancy Tommye; Jordan, John Douglas
     Concepto Diagnostics, USA
PA
SO
     PCT Int. Appl., 24 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM G01N033-543
CC
     9-1 (Biochemical Methods)
     Section cross-reference(s): 13, 15
FAN.CNT 1
     PATENT NO.
                     KIND DATE
                                          APPLICATION NO. DATE
     ---<del>-</del>-----
                     ____
                            -----
                                           -----
PΙ
     WO 9939208
                      A1
                           19990805
                                          WO 1999-US2331
                                                           19990202
            AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
            KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
            MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
            TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
            TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2319417
                      AA
                           19990805
                                          CA 1999-2319417 19990202
    AU 9925795
                      A1
                           19990816
                                          AU 1999-25795
                                                            19990202
    EP 1053473
                      A1
                           20001122
                                          EP 1999-905689
                                                           19990202
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
    BR 9908550
                      Α
                           20001128
                                          BR 1999-8550
                                                           19990202
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JP 2002502036
                      T2
                           20020122
                                         JP 2000-529611
                                                          19990202
    US 2001024799
                      A1
                           20010927
                                         US 2001-764826
                                                          20010117
PRAI US 1998-16995
                      Α
                           19980202
    WO 1999-US2331
                      W
                           19990202
    The present invention provides
                                    ***antibodies***
                                                       which specifically
AB
    bind ***early*** ***conception*** ***factor*** , which can be
    found in body fluids of animals including but not limited to the cow, cat,
    dog, horse, human, sheep, and pig. The invention provides methods for
    detecting conception or the absence of conception in an animal, the latter
    being recognized by the absence of ***early***
                                                        ***conception***
                    in a suitable body fluid collected from the animal.
       ***factor***
    Apparatus for detecting ***early***
                                             ***conception***
       ***factor*** in a body fluid from an animal comprising the
       ***antibodies***
                       which specifically bind ***early***
                           ***factor*** are also provided.
       ***conception***
ST
       ***early***
                      ***conception***
                                         ***factor***
                                                           ***antibody***
    app fertilization
IT
     Immunoglobulins
    RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BPR
     (Biological process); BSU (Biological study, unclassified); PRP
     (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
        (A, monoclonal, to
                           ***early*** ***conception***
        ; method and app. for detecting conception in animals using
         ***antibodies***
                          ***conception***
         ***factor***
IT
    Glycoproteins, specific or class
    RL: ANT (Analyte); BPR (Biological process); BSU (Biological study,
    unclassified); BUU (Biological use, unclassified); PUR (Purification or
    recovery); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
        (ECF ( ***early***
                             ***conception***
                                                 ***factor*** ); method
       and app. for detecting conception in animals using ***antibodies***
            ***early***
                           ***conception***
                                                ***factor*** )
IT
     Immunoassay
        (app.; method and app. for detecting conception in animals using
         ***antibodies***    to    ***early***       ***conception***
         ***factor***
IT
     Insemination, artificial
        (assay for ***early***
                                  ***conception***
                                                        ***factor***
                                                                       in
       humans and cows in relation to; method and app. for detecting
       conception in animals using
                                   ***antibodies*** to
                                                            ***early***
                            ***factor*** )
         ***conception***
ΙT
       ***Antibodies***
    RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical
    study); BIOL (Biological study); PROC (Process); USES (Uses)
                                      ***conception***
        (chimeric, to ***early***
       method and app. for detecting conception in animals using
         ***antibodies*** to ***early*** ***conception***
         ***factor*** )
IT
       ***Antibodies***
    RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical
    study); BIOL (Biological study); PROC (Process); USES (Uses)
                        ***early***
                                    ***conception***
        (conjugates, to
                                                             ***factor***
       with detectable group; method and app. for detecting conception in
                      ***antibodies*** to
       animals using
                                              ***early***
         IT
    Blood analysis
    Blood serum
    Body fluid
        ***Milk***
                   analysis
```

```
Urine analysis
          ***early***
                         ***conception***
                                               ***factor***
                                                              detection in;
       method and app. for detecting conception in animals using
          ***antibodies***
                           to
                                 ***early***
                                                 ***conception***
          ***factor***
IT
     Cat (Felis catus)
     Cattle
     Dog (Canis familiaris)
     Horse (Equus caballus)
     Swine
          ***early***
                         ***conception***
                                              ***factor***
                                                              of; method and
        app. for detecting conception in animals using ***antibodies***
          ***early***
                         ***conception*** ***factor*** )
IT
    Hybridoma
        (for monoclonal
                         ***antibodv***
                                          prodn.; method and app. for
        detecting conception in animals using ***antibodies***
                                              ***factor***
          ***early***
                        ***conception***
IT
       ***Antibodies***
    RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical
     study); BIOL (Biological study); PROC (Process); USES (Uses)
        (humanized, to ***early***
                                        ***conception***
                                                             ***factor***
       method and app. for detecting conception in animals using
          ***antibodies***
                           to ***early***
                                                ***conception***
          ***factor***
       ***Antibodies***
IT
    RL: ARG (Analytical reagent use); DEV (Device component use); SPN
     (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study);
    BIOL (Biological study); PREP (Preparation); USES (Uses)
                          ***early***
                                          ***conception***
        (immobilized, to
       method and app. for detecting conception in animals using
          ***antibodies***
                           to ***early***
                                                ***conception***
          ***factor***
IT
    Animal
    Fertilization
     Immunoassay
        (method and app. for detecting conception in animals using
          ***antibodies***
                           to ***early*** ***conception***
          ***factor***
IT
       ***Antibodies***
    RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU
     (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (monoclonal, conjugates, to ***early***
                                                     ***conception***
                       , with colloidal gold; method and app. for detecting
          ***factor***
       conception in animals using ***antibodies*** to ***early***
                              ***factor*** )
          ***conception***
IT
       ***Antibodies***
    RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BPR
     (Biological process); BSU (Biological study, unclassified); PRP
     (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
        (monoclonal, to ***early*** ***conception***
                                                              ***factor*** ;
       method and app. for detecting conception in animals using
         ***antibodies***
                           to ***early***
                                              ***conception***
         ***factor***
IT
    Membranes, nonbiological
        (nitrocellulose, with immobilized ***antibodies***
                                                              to
                                                                   ***earlv***
                             ***factor*** ; method and app. for detecting
         ***conception***
       conception in animals using ***antibodies*** to ***early***
         ***conception***
                             ***factor*** )
IT
       ***Antibodies***
```

```
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BPR
     (Biological process); BSU (Biological study, unclassified); THU
     (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP
     (Preparation); PROC (Process); USES (Uses)
             ***early***
                           ***conception***
                                               ***factor*** ; method and
       app. for detecting conception in animals using ***antibodies***
         7440-57-5D, Gold, conjugates with ***antibody*** to
IT
                                                          ***earlv***
      RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
    study); BIOL (Biological study); USES (Uses)
       (colloidal; method and app. for detecting conception in animals using
         ***antibodies***
                         to ***early***
                                            ***conception***
         ***factor***
IT
    9003-99-0D, Peroxidase, conjugates with ***antibody***
                                       ***factor***
      ***early***
                     ***conception***
    RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
    study); BIOL (Biological study); USES (Uses)
       (horseradish; method and app. for detecting conception in animals using
         ***antibodies*** to ***early*** ***conception***
         ***factor***
IT
    9004-70-0D, Nitrocellulose, with immobilized anti- ***early***
                         ***factor*** ***antibodies***
      ***conception***
    RL: DEV (Device component use); USES (Uses)
       (membrane; method and app. for detecting conception in animals using
         ***antibodies***
                          to ***early***
                                             ***conception***
         ***factor***
    9001-78-9D, conjugates with ***antibody*** to
IT
                                                    ***early***.
                         ***factor***
***early***
      ***conception***
                                         9002-13-5D, Urease, conjugates with
      ***antibody*** to
                                         RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
    study); BIOL (Biological study); USES (Uses)
       (method and app. for detecting conception in animals using
                         to ***early***
         ***antibodies***
                                             ***conception***
         ***factor***
RE.CNT
             THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) May; US 5602040 A 1997 CA
(2) Quinn, K; Cancer Immunology Immunotherapy 1992, V34, P265 CA
=> logoff y
COST IN U.S. DOLLARS
                                             SINCE FILE
                                                            TOTAL
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FULL ESTIMATED COST
                                                  94.42
                                                            94.63
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
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                                                            TOTAL
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-24.80

-24.80

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